SíMA

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Abstract

Simple Medicine Applicator
We are four students from the inno.space design factory at the University of Applied Sciences in Mannheim. As Team Bee we are part of the design thinking challenge CBI A^3, which challenged us to connect the UN Sustainable development goal number three "Good health and wellbeing" with the unique technologies from CERN to create soultions for the year 2030.
This whitepaper presents the first concept for our idea called SiMA (Simple Medicine Applicator), designed to stop the further development of antibiotic resistant germs. This is going to have a high societal impact, because by 2050 drug resistant infections will kill an extra 10 million people a year worldwide - more than currently die from cancer.

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1 Societal Challenge

"The world is heading towards a post-antibiotic era in which common infections will once again kill. If current trends continue, sophisticated interventions, like organ transplantation, joint replacements, cancer chemotherapy and care of pre-term infants, will become more difficult or even too dangerous to undertake. This may even bring the end of modern medicine as we know it." **Dr. Margaret Chan** [1]

The overuse of antibiotics has led them to become less and less effective to treat us when we are sick - leaving scientists scram. Drug resistant infections will kill an extra 10 million people a year worldwide - more than currently die from cancer - by 2050, unless action is taken. Antibiotic resistant germs are currently implicated in 700,000 deaths each year. [2]
The world is nearing a moment when antibiotics no longer work to treat infections. We are severely overusing and misusing the antibiotics we have – and that system is causing bacteria to evolve and develop resistance to the drugs intended to kill them. Appropriately, the phenomenon is referred to as antibiotic resistance, and it is shaped up to be one of the biggest challenges we face in the 21st Century. [3]
But this development did not happen without pre-warning. Alexander Fleming, who discovered penicillin in 1946, already warned of such a development. He feared that the general public does not realize the real value and dangers of antibiotics and that the bacteria could develop better defenses and resistances through reckless overuse. [1]

"The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. [...] I hope the evil can be averted." **Alexander Flemming** [1]

The good news? A whole range of governments, organizations, innovators, and scientists across the globe is pondering how to get us out of this mess, they are already working on future solutions, for example they are planning to:

- use infectionkilling polymers
- make existing antibiotics stronger
- deploy tiny semiconductors into the body or
- use bacteria against itself

But unfortunately, all these methods have one big problem: it is a long time until they will be ready to use. Now we need to win as much time as possible until new technologies are fully developed and tested to be safe for human treatment.
This is where our product comes in: the simple medicine applicator SiMA, which was designed to prevent the development of multiresistant germs caused by the misuse and overuse of antibiotics using an idea that has not yet been considered. [3]

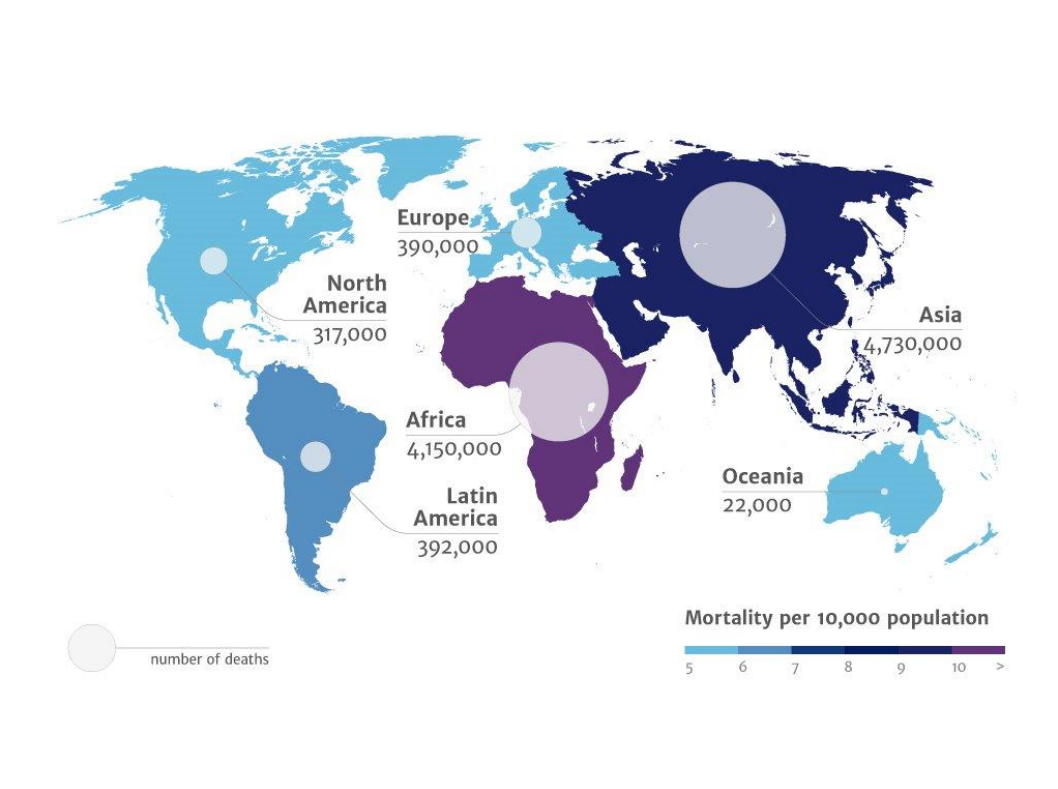

Figure 1.1: Number of deaths due to antibiotic resistance in 2050 [4]

2 Conceptual design

The Simple Medicine Applicator (SiMA) is a bracelet which contains medicine and administers it trans dermal. SiMA resembles a modern smart watch. There is a drug container attached which holds the medicine required for treatment. This container can only be accessed by the doctor. The patient has to wear the bracelet for the whole duration of the treatment. The major benefit is that patients no longer have to remember to take the medicine at the right time and that it is therefore impossible for them to forget taking it or to stop the treatment intentionally. With integrated sensors it measures and monitors the current health state and concentration of the medicine in the blood and checks if the body responds to the treatment, so the dose can be personalized. In case of any side effects the doctor will be informed and can induce change in the dose or medicine.
With this device we are aiming to avoid a misuse of medicine, especially antibiotics. Furthermore SiMA realizes a personalized treatment which is important because patients with identical diseases can have different responses to the same therapy and dose of medicine like antibiotics. This is caused by different endowments of the respective organism with enzyme variants that degrade antibiotics or other drugs at different rates.
An overuse of antibiotics causes stress on the kidney and the liver, but an unfinished treatment leads to multi-resistant germs. Additionally, alternative substances for antibiotic resistance are more toxic and expensive. [5] That's why we want to personalize antibiotic therapy with SiMA and define the end of the treatment based on individual response of the body.
A reduced use of antibiotics, a lower therapy failure rate, the stop of the development of multi-resistant germs, the misuse of drugs and a decrease of side-effects are some benefits for good health and well-being we want to achieve with SiMA.

2.1 Interaction of components

In general, our concept consists of four main parts: a rapid blood test to identify the bacteria causing the disease, the medication bracelet to cure the disease, biosensors to check the response of the body to the therapy and data processing to monitor the concentration in the blood and personalize the therapy.

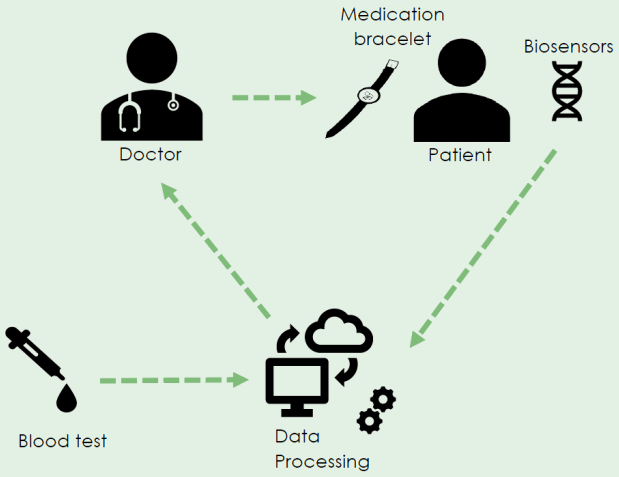

Figure 2.1: component interaction

2.2 Rapid blood test

For now the sick patient has to visit the doctor first. If the doctor detects through his anamnesis that the patient needs an antibiotic, a rapid blood test is carried out for example by mass spectroscopy. This should provide information about the exact characteristics of the bacterium and its concentration in the blood. The test result is then fed into data processing to provide the doctor with a suggestion for the right antibiotic and start dose.

2.3 Medication bracelet

If the right antibiotic is found the patient will receive a medicine bracelet, which he will have to carry for the whole duration of the treatment. To protect the privacy of the patient, the design of the medication bracelet is very similar to a normal

smartwatch. The bracelet consists of the following components:

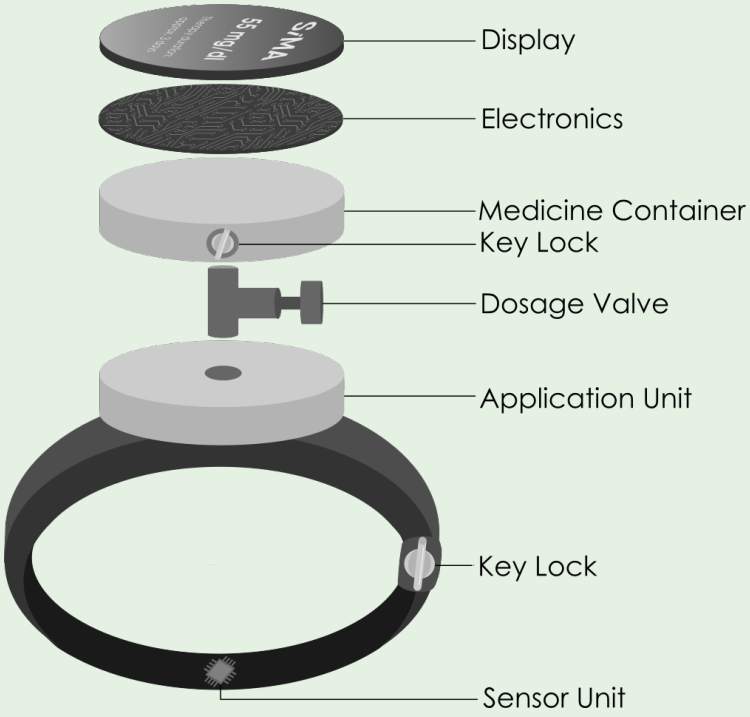

Figure 2.2: components of the medication bracelet

Display

The Display will always inform the patient about its medication and health state. It will display the current dose of the medicine and the estimated cure time. In case of any severe problems with the disease or the medication a message will be shown to advise the patient to visit the doctor. To ensure that the therapy will be most effective the display will moreover show recommendations for actions for the duration of the therapy. This is important due to the fact that antibiotic has a big influence on the body and may reduce for example the effect of the contraceptive pill or make the body more light sensitive.[6]
Since Sima will measure vital functions as well the display can additionally function as a normal smart watch and show for example the pulse or blood pressure.

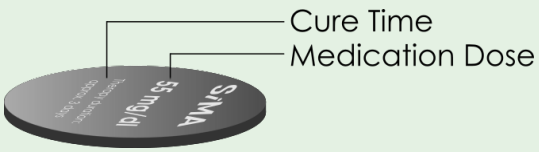

Figure 2.3: Display

Electronic Layer

The electronic layer will be placed underneath the display and will provide power supply for all components and will function as the gateway for wireless communication. The central element of this part is the control unit. It will receive the encrypted therapy data and will provide this information to all the other parts of the bracelet. It will control the dosage through the regulation of the dosage valve and will contain all necessary data that is needed by the display. In case of any therapy changes, the control unit will receive this information immediately and the regulation will be adjusted. Additionally, the control unit will receive data from the bracelet elements for example the filling state of the medicine container and the measurement results from the sensor unit. In case of any malfunctioning of any part of the bracelet the control unit will get this data as well. The collected data will be encrypted and sent to the data processing for further analyzes. The function of the control unit can for example be realized by a micro controller.

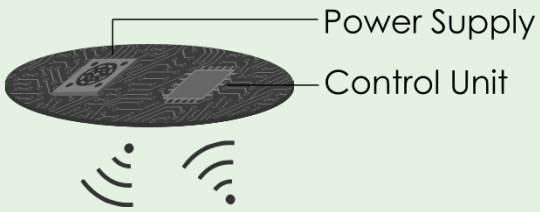

Figure 2.4: Electronic Layer

Medicine container

Before the bracelet is attached to the patient's arm the medication container has to be fill by the doctor. The container can only be opened and closed by a doctor using a specific key. This prevents the drugs from being misused. The drugs are filled in as powder. The medication container is hermetically sealed and only has a connection to the dosage control unit that is placed underneath. In addition, the medicine container is equipped with a level sensor that will measure the filling state of the medicine. In case the amount of antibiotics that is left in the container is to low, the patient will be informed via the display and the doctor will receive a notification as well so that the container can be filled again. This procedure guarantees that the therapy does not have to be interrupted at any time.

Dosage valve

The dosage valve is used as the connector unit between the medicine container and

the application unit. The valve is regulated by the control unit of the electronic layer. The control unit will send impulses to the valve at a regular interval which will open the valve so that the medicine in the container can be forwarded to the application unit to ensure continuous medication Additionally, to the dose regulation the valve will separate the medicine container form the application unit. This has the big advantage that unused medication can be removed from the container after therapy and can be reused, as it has not been in direct contact with the patient.

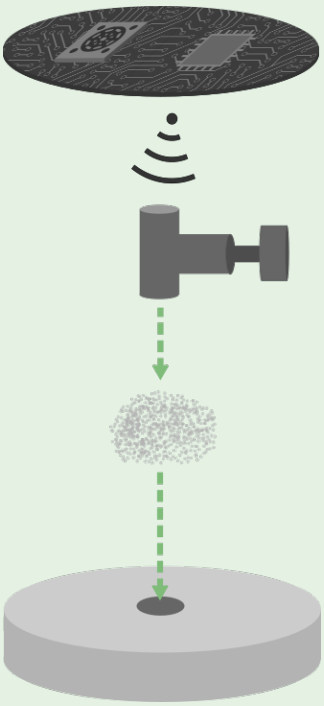

Figure 2.5: Dosage Valve

Medicine application unit

The medicine that was forwarded to the application unit is processed there so that the drugs can be absorbed through the skin. In general, it is possible to absorb antibiotics trans dermal. There are already antibiotic ointments available these days. [7], [8]

On the bottom side of the application unit a semi permeable membrane is located, which ensures that the drugs can be released from the inside of the unit to the skin, but sweat or other particles from the outside cannot get into the unit. The continuous application on the one hand leads to a constant level of medication in the blood and makes the dosage more tolerable as it is not intermittent. On the other hand, there is no need for taking pills anymore, an incorrect intake or the

forgetting of it is therefore no longer possible.

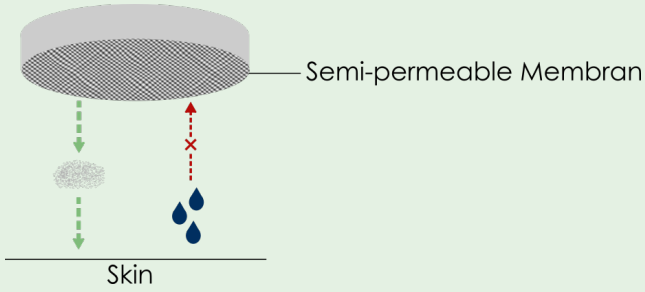

Figure 2.6: Application Unit

Sensor unit

The sensor unit is used to control the effect of the medicine on the body. It consists of two parts, a readout unit for the biosensors and a vital function monitoring unit. The biosensor readout unit will measure the signal of the antibiotic concentration and the therapy effectiveness. The measurement will be done by an electronic detector and an amplifier. The data will be sent to the control unit which will encrypt it and send it to data processing for therapy adjustment. Since the application of the antibiotic will be done on the top side of the wrist, the sensor unit is integrated in the watch strap so that the measurement can be done at the anterior side of the wrist.

The vital function monitoring unit will monitor the health state of the patient. It will detect any side effects or medicine intolerances. In this case the medication can be stop wireless by the doctor and the medication can be adjusted which will require another doctor visit. This will ensure that the new medication therapy will not have any negative effects on the user. Moreover, the general health state can be monitored so that any health deterioration can be detected as quickly as possible and further therapies can be initiated. An improvement in the general state of health can also provide information about the effectiveness of the therapy.

Figure 2.7: Sensor Unit

2.4 Biosensors in the blood

Depending on the disease specific biosensors are given to the patient which will monitor the concentration of the medicine in the blood as well as the effectiveness of the treatment. The dose of the antibiotics in the blood is measured to control the absorption of the antibiotic, since it is unique for every patient and depended on factors like age, gender or the body fat content. Due to this specific absorbance, every patient requires an individual dose, which can only be precisely determined after the start of the therapy. [5] To avoid regular blood tests or stabbing the finger the biosensors are used and injected into the blood when the therapy is started. A biosensor is a measuring device that consists of a biological active sensor or receptor and a transducer. The molecules that are wanted to be detected will react with the specific receptor of the biosensor. This reaction will cause a biochemical or optical reaction that will be detected by the transducer and transformed to an electrical signal. Depending on higher or lower concentration more or less biosensors will react which will affect the quantity of the electric signal produced by the transducer. [9]
This signal will be measured by the sensor unit of the bracelet and the concentration of antibiotics in the body can be determined. In this way the concentration can be measured continuously without any inconveniences for the patient.
A second set of biosensors is needed to control the effectiveness of the medication. In case of antibiotics the concentration of the protein Procalcitonin (PCT) can be measured. PCT is a protein that occurs in higher concentrations in the body during severe bacterial, fungal and parasitic infections. In case the antibiotic is effective the PCT concentration in the blood will decrease and the therapy end can be determined individually after the concentration is fallen under a certain level. [10] The PCT biosensor will work in the same way as the antibiotic concentration sensor.

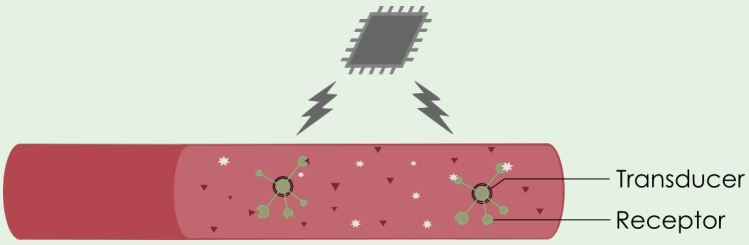

Figure 2.8: biosensors in the blood

2.5 Data processing

Data processing is needed at two points. At the beginning of the therapy it is used to identify the best antibiotic to cure the specific disease. The results of the blood test are fed into data processing and the characteristics of the bacterium are compared with the entries in a database, from which the most effective antibiotic for the specific bacterium is selected. In addition, the individual aspects of the patient such as intolerances, medication history or interactions with other medications already being taken, are considered. This will ensure a personalized antibiotic therapy. In the end the doctor will get a suggestion of the best antibiotic and a start dose for the therapy that will lead to the most promising result.
During the therapy data processing is continuously used to monitor the effectiveness of the therapy and the health state of the patient. For this the information from the sensor unit is collected and compared to expected values. In case of too large deviations suggestions for dose or therapy changes are given to the doctor. As for severe problems like intolerances or serious side effects an emergency protocol will be executed that will immediately stop the medication and alarm the doctor. This will always ensure the security of the patient.

Figure 2.9: Data processing

2.6 Users and touchpoints

Our concept will be available for everyone who needs a treatment with antibiotics. The needed medicine is filled in the container of SiMA by the doctor to ensure the correct mediaction and that the patient takes the medicine.
SiMA helps the doctors to monitor the therapy even when the patients are not in the practice or hospital. This keeps freedom for the patient, while the doctor has the possibility to check the health status at any time. Moreover, they can arrange appointments only when they are needed which will improve the time management of the doctor.
Research institutes in pharmaceutical industry dealing with effects of antibiotics can have access to the measured data which is collected during a treatment. They get the opportunity to optimize and further develop medicines, for example to reduce side effects.
The health insurance company also benefits from SiMA, as it lowers the consumption of certain drugs and reduces the duration of therapy due to less frequent side effects.

3 CERN Technologies

For SiMA two CERN Technologies will be used: REMUS and ROOT.
Remus is a System, which was originally designed to monitor the environment of the CERN facilities. For SiMA it will be used to monitor the environment of the body throughout sensors. It will provide a unified way to supervise and continuously operate heterogeneous types of instrumentation. In Addition REMUS is able to display near real-time meassurements and alarms. Finally it supports customisable user interfaces making SiMA easy to handle for users with non technological backgrounds, like doctors and patients. [11], [12]
The second technology integrated in SiMA will be ROOT. This framework is able to handle and analyze large amounts of data extremely efficient. This will be used to analyse, store and query the data collected by the sensors. [13], [14]

4 Value of conceptual Design

We are convinced that our concept will have a large societal impact on everybody, because it will prevent the misuse and accidental wrong mediaction of antibiotics. This is going to stop the fruther creation and development of multi resistant germs, because our research has shown, that not the detection but the ongoing misuse and treatment errors are the reason we are losing the fight against multi resistant germs. As a conclusion of this SiMA ensures that diseases like lung infections will still be curable by antibiotics in 2030.
Furthermore we believe, that our concept has the potential to be further developed and expanded towards other drugs. Especially those who are highly misused, addictive or difficult to medicate, for example opiodes.

5 Conclusion and further development

In conclusion our team is confident, that SiMA will have a measurable impact on good health and well being of our society in the near future. For the next phase we are planning to iterate our concept by:

- conducting research on transdermal application of other medicine
- conduction research on laws concerning medication
- creating a roadmap for the realization of SiMA
- interview specialists on the usage of CERN and biosensor technologies
- iterating our prototype

Further we are planning to expand our user groups towards people suffering from chronic diseases, who can also benefit from SiMA, because it makes therapy easier for them and they do not always have to think about medication and therefore maybe less about the disease itself. Elderly people may also have to take a lot of different drugs several times a day. This can easily become complicated and these people are usually dependent on another person to keep track and ensure that the medication is taken correctly. Old people usually refuse to take medication or simply forget to do so. With SiMA this can be prevented. Another possible target group are hospitalized people, who need to take medicine several times a day. For instance, after severe operations, when it is difficult to swallow medicine an infusion can be avoided.This is gonig to strongly increase the societal value of our concept in the future.

6 Our Team

Our Team consists out of four students from the inno.space design factory Mannheim: Christian, Hannah, Kristina and Sarah. Together we are an interdisciplinary team, that combines engineering and design skills to solve the given challenge. So without furhter a due meet the members of Team Bee:

Sarah Lottner

Biomedical Engineering

"I am a second semester master student of Biomedical Engineering at the University of Applied Sciences in Mannheim. I started studying Medical Engineering, because I wanted to combine my interests in engineering with the wish of helping people with my work. I'm really happy now to be part of the CBI program which focuses on exactly this."

Kristina Markl

Biomedical Engineering

"I am a Biomedical Engineering master student in my second semester at University of Applied Sciences Mannheim. I can relate to the Sustainable Goal 'Good Health and Well-being' of the UN because of the link to the field of study Biomedical Engineering and I'm looking forward to build Challenge Based Innovation pilots to combine own ideas and skills with CERN technology."

Hannah Teufel

Biomedical Engineering

"I am a first semester student in the masters program of Biomedical Engineering at the University of Applied Sciences in Mannheim. I chose to be a part of CBI because it is inspiring to get to know so many new technologies, people and perspectives."

Christian Wuckert

Communication Design

"Good health and wellbeing is something we completely forget about as long as we feel fine, but It actually is the most important aspect of our lifes. I got on board because the question, what do people consider wellbeing and how it impacts their overall health, in a physical and psychical way, occupies me. Investigating and using CERN technology to possibly solve one or multiple existing problems of goal no.3 would be great!"

7 Our Partners

The Challenged Based Innovation Program CBI A^3 is powered by CERN IdeaSquare and the design factory Melbourne at Swinburne University. Apart from inno.space design factory Mannheim they are collaborating with the New York City design factory at Pace University this year.

List of Figures

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